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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte SANDRINE LENTSCH GRAF,
JEAN RENE CARTIER and CLAUDINE CARTIER

Appeal 2008-2710
Application 09/937,103
Technology Center 1600

Decided: August 15, 2008

Before DONALD E. ADAMS, RICHARD M. LEBOVITZ, and FRANCISCO C. PRATS, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 9, 10, and 16. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

The claims are drawn to a method of preserving the immunogenicity of a liquid vaccine composition. The method steps involve combining the vaccine with trehalose, which is characterized in the Specification as a known "cell protectant" (Spec. 5: 5-6). The Specification does not define the term "immunogenicity," but it would be understood from reading the Specification that "immunogenicity" refers to the ability of the vaccine to elicit an immune response (Spec. 8: 24 to 9: 16).

Claims 9, 10, and 16 stand rejected under 35 U.S.C. § 103(a) as obvious over Samaritani (WO 96/29095, published Sept. 26, 1996), Sola-Penna (ARCH. BIOCHEM. BIOPHYS., 360: 10-14, 1998), and Anderson (U.S. Pat. No. 5,097,020, issued Mar. 17, 1992) (Ans.[1] 3).

We select claim 9 as representative of the appealed claims. Claims 10 and 16 fall with claim 9 because separate reasons for their patentability were not provided. 37 C.F.R. § 41.37(c)(1)(vii). Claim 9 reads as follows:

> A method of preserving the immunogenicity over time of a liquid vaccine composition comprising at least one antigen consisting of a polysaccharide bound to a carrier protein, wherein the method comprises combining in a liquid (a) trehalose and (b) the antigen to form a liquid vaccine composition, and storing the vaccine composition in the liquid state.

ISSUE

The Examiner finds that the prior art teaches protecting liquid compositions comprising proteins from degradation by combining them with a sugar. The Examiner also finds that the sugar trehalose was known to stabilize proteins. Based on these teaching, the Examiner takes the position

[1] "Ans." refers to the Examiner's Answer mailed Aug. 3, 2007.

that persons of ordinary skill in the art would have been prompted to combine a prior art vaccine with trehalose to have made the claimed invention. Appellants contend that there would have been no motivation to have combined the prior art in the manner suggested by the Examiner. Therefore, the issue in this appeal is whether the Examiner erred in concluding that it would have been obvious to have combined the prior art teachings to have made the claimed invention.

Scope and content of the prior art

In making an obvious determination, the Examiner must first identity the scope and content of the prior art and then ascertain the differences between the prior art and the claimed invention. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). Thus, we first turn to the prior art. The following numbered findings of fact ("FF") summarize the prior art relied upon by the Examiner in setting forth the basis of the rejection (Ans. 3-5):

SAMARITANI

1. Samaritani states that it "is known that highly purified proteins easily undergo degradation, even due to the contact with atmospheric agents" (Samaritani, at 1, ll. 7-8).

2. Samaritani acknowledges that "[n]o liquid stabilised formulations of gonadotropins have been described until now" (Samaritani, at 1, ll. 22-23).

3. Samaritani describes a liquid formulation hCG (human Chorionic Gonadotropin) stabilized with a polyalcohol or a non-reducing sugar (Samaritani, at 1, ll. 3-6).

SOLA-PENNA

4. According to Sola-Penna:

> Trehalose has been described to act as the best stabilizer of structure and function of several macromolecules. Although other sugars also stabilize macromolecules, none of them are as effective as trehalose.

(Sola-Penna, at 10 (Abstract); at 13, col. 1; *see* Ans. 4.)

5. Sola-Penna states that trehalose protects cells, cell membranes, and proteins against stress conditions (Sola-Penna, at 10, cols. 1-2).

6. Sola-Penna also states that trehalose also has been shown to modulate enzyme activity and protect against thermal inactivation (Sola-Penna, at 10, cols. 1-2).

7. Experiments were performed by Sola-Penna to explain why trehalose has higher efficiency in stabilizing macromolecules and modulating enzyme activity than other sugar molecules (Sola-Penna, at 10, col. 1; at 13, col. 2).

8. The experiments involved measuring the ability of trehalose and other sugars to protect against enzymes against thermal inactivation (Sola-Penna, at 10, col. 1).

ANDERSON

9. Anderson teaches a vaccine comprising bacterial capsular polymers attached to protein carriers (Ans. 4).

Difference between the prior art and the claimed invention

Once the scope and content of the prior art has been determined, the next step is to identify the differences between the prior art and the claimed invention. *Graham*, 383 U.S. at 17. The following numbered findings of fact are pertinent to this issue:

10. Claim 9 is directed to a method "of preserving the immunogenicity over time of a liquid vaccine."

11. The vaccine composition comprises "at least one antigen consisting of a polysaccharide bound to a carrier protein."

12. The method has two steps:

13. "combining" (a) trehalose and (b) the antigen in a liquid to form a vaccine composition; and

14. "storing the vaccine composition in the liquid state."

15. The preamble of claim 9 states that the method is for "preserving the immunogenicity over time of a liquid vaccine composition." In other words, the purpose of combining the trehalose and the antigen is to preserve the resulting vaccine's immunogenicity when stored.

Thus, the preamble merely states a purpose or intended result of the process which is set forth in the body of the claim (i.e., FF14-15), rather than impart a manipulative step or other difference that would limit how the process is carried out.[2]

16. Samaritani describes combining a protein with a sugar to protect it from degradation (FF1-3) and storing it in a liquid state (*see* FF2, 3), but does not describe the sugar as trehalose nor the protein as a vaccine component comprising a polysaccharide bound to a protein as required by claim 9 (FF11, 13).

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[2] It is well-established that claim language which states a purpose and intended result of a claimed method does not limit the scope of the claim. *Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc.*, 246 F.3d 1368, 1372 (Fed. Cir. 2001). Preamble language that merely states the purpose or intended use of the claimed subject matter is generally not treated as limiting the scope of the claim. *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1345 (Fed. Cir. 2003); *Rowe v. Dror*, 112 F.3d 473, 478 (Fed. Cir. 1997).

17. Anderson describes a vaccine composition (FF 9) that meets the limitations of the antigen recited in claim 9 (Ans. 4-5).

Reason to combine the prior art

Once the differences between the prior art and the claimed invention have been ascertained, the next step is to identify a reason why persons of ordinary skill in the art would have been prompted to combine the prior art to have made the claimed invention. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007). The following findings are relevant to this determination:

18. Based on Samaritani's teaching that purified proteins undergo degradation and that sugars are useful to address this problem (FF1, 3), persons of ordinary skill in the art would have been prompted to add a sugar to Anderson's vaccine composition (FF9) which contains protein in order to stabilize it against degradation (*see* Ans. 4-5)

19. Sola-Penna teaches that the sugar trehalose is known to be the "best stabilizer of structure and function of several macromolecules" (FF4) and is also known to protect cell, membranes, proteins, and enzymes (FF5, 6).

20. Consequently, persons of ordinary skill in the art would have been prompted to replace the sugar taught by Samaritani with trehalose for its known and expected benefit (FF4-6, 19) in stabilizing proteins, including Anderson's vaccine composition (Ans. 5).

21. Thus, the prior art would have suggested substituting trehalose (FF20) and antigen consisting of a polysaccharide bound to a carrier protein (FF18) in Samaritani's method to have made the claimed invention.

Analysis

During patent examination, the examiner bears the initial burden of establishing a prima facie case of obviousness. *In re Kumar*, 418 F.3d 1361, 1366 (Fed. Cir. 2005). In setting forth a case of obviousness, "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does . . . because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. at 1741.

After reviewing the scope and content of the prior art and the reason for combining it, we conclude that sufficient evidence has been provided to establish prima facie obviousness of claim 9. The differences between Samaritani and the claimed invention are that Samaritani does not use trehalose to stabilize a liquid vaccine comprising a polysaccharide bound to a protein (FF16). However, Sola-Penna teaches the superiority of the sugar trehalose for stabilizing macromolecules (FF4, 7, & 19), providing a strong reason to have used it in Samaritani's method (FF20). Samaritani also teaches that proteins are susceptible to degradation (FF1). Thus, persons of ordinary skill in the art would have recognized that Anderson's vaccine comprised of protein would benefit from the combined teachings of Samaritani and Sola-Penna (FF18-21).

Appellants contend that there is no suggestion or motivation to have combined the prior art. They argue that the cited references are not concerned with the effects of a sugar on the immunogenicity of an antigen (App. Br. 6).

This argument is not persuasive. We agree that there is no explicit teaching in Samaritani about preserving a protein's immunogenicity. However, "immunogenicity" appears only in the claim's preamble. In this context, it is recited as a purpose or intended result of the claimed process (FF15). Since the claimed process steps are completely suggested by the prior art, and the preamble does not impart any additional structures or manipulative steps to the claimed process (FF15), we do not find that the preamble is sufficient to distinguish the claimed method from the prior art. Consequently, we do not agree that a "connection between (a) thermal stability and (b) immunogenicity of polysaccharide-protein conjugates" is necessary to establish prima facie obviousness of the claimed subject matter as asserted by Appellants (Reply Br. 2).

Appellants argue that "Sola-Penna et al. provides a study of trehalose as a stabilizer of 'macromolecules,' but the only macromolecules considered are enzymes and the stabilization studied was with respect to thermal effects on enzymatic activity" (App. Br. 6). This argument is also not persuasive. Sola-Penna quite clearly characterizes trehalose as the best stabilizer of macromolecules, noting its known efficiency in stabilizing proteins in different environments (FF4-6). Therefore, persons of ordinary skill in the art would not have read Sola-Penna as teaching trehalose's only use is to protect enzymes against thermal inactivation. While Sola-Penna's experiments involved the effect of trehalose on thermal inactivation, this was only to experimentally determine the mechanism responsible for trehalose's "higher efficacy" in stabilizing proteins in comparison to other sugars (FF8). Given Sola-Penna's broader statements about the benefits of trehalose (FF 4,

5), we find that the preponderance of the evidence favors the Examiner's position.

We also not find Samaritani's teaching about the hCG hormone to restrict its method to hormones as Appellants contend (App. Br. 7). Samaritani states that degradation was a problem associated with purified proteins (FF1) and, thus, explicitly teaches that proteins other than hCG are susceptible to degradation, which would include Anderson's vaccine comprising protein. In sum, we see no infirmity in the Examiner's logic extending Samaritani's teaching to Anderson's vaccine.

For the foregoing reasons, we affirm the rejection of claim 9. Claims 10 and 16 fall with claim 9.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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